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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/762,447

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Stanton McHardy

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PFIZER INC.

PATENT DEPARTMENT, MS8260-1611

EASTERN POINT ROAD

GROTON, CT 06340

EXAMINER

CHANG, CELIA C

ART UNIT

PAPER NUMBER

1625

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

03/16/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/762,447	<b>Applicant(s)</b> MCHARDY ET AL.	
	<b>Examiner</b> Celia Chang	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 17 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-7,9,10,20-24 and 28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7,9,10,20-24 and 28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. Applicant's election with traverse of Group I with species CP-775356-01, p.30 lines 14-15, in the reply filed on Aug. 17, 2006 is acknowledged. The traversal is on the ground that the method of treating claims should be rejoined. To the extent that the method claims which depend solely on the elected compounds and free from any 112 issues, they are rejoined and the restriction between the elected compounds and their method of use is hereby withdrawn.

The requirement is still deemed proper and is therefore made FINAL.

Claims 8, 11-19, 25-27, 29 have been canceled. Claims 1-7, 9-10, 20-24, 28 are pending.

#### 2. *Oath/Declaration*

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application, by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state that the person making the oath or declaration has reviewed and understands the contents of the specification, including the claims, as amended by any amendment specifically referred to in the oath or declaration.

It does not identify the city and either state or foreign country of residence of each inventor. The residence information may be provided on either an application data sheet or supplemental oath or declaration.

3. Claims 1-7, 9-10, 20-24, 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are indefinite where R3 and R5 are defined as optionally being a substituted or unsubstituted "C1-C6 cycloalkyl". A cycloalkyl group would require at least three carbons and therefore it is unclear what the term "cycloalkyl" means.

Claims 1-7, 9-10, 20-24, 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims are indefinite where formulas I and II do

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not clearly define what chemical moiety is in the parentheses, “( )n”. It is unclear whether the moiety within the parentheses is a methylene group or some other chemical moiety. The scope of the instant claims cannot be ascertained due to the ambiguity of the parentheses notation.

Claims 1-17, 20-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims are indefinite where R3 and R5 are optionally a “substituted alkyl” or “substituted cycloalkyl” for which no substituents have been given. The metes and bounds of substituted by what cannot be ascertained reading in light of the specification (see specification pages 10-11).

4. Claims 2-7, 9-10, 20-24, 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are indefinite where a compound according to claim 1 wherein “the preferred relative stereochemistry” between R6 and R7 is *trans* is claimed.

The term “preferred” in claim 2-7, 9-10, 20-24, 29 is a relative term which renders the claim indefinite because one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear whether the compound being claimed is the compound wherein the relative stereochemistry between R6 and R7 is *trans* or if the instant claimed compound can be either a *trans* or *cis* relative stereochemistry between R6 and R7, but *trans* is preferred. If it is inclusive of both *trans* and *cis*, then, claim 2 is a duplicate of claim 1.

5. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is indefinite where a pharmaceutical composition comprising an “effective amount” of a compound according to claim 1 is claimed. The claim is indefinite because an effective amount cannot be ascertained. Please note the scope of the claim is for a composition comprising a quantity which will treating a disease mediated i.e. both antagonistic and agonistic affect the opioid receptor and modulate i.e. inhibitory or enhancing the opioid receptor. It is unclear what amount such “effective amount” would be. A single compound cannot simultaneously both inhibit and enhance receptor activity. The instant claim is indefinite

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because it unclear how the opioid receptor mediates a disease state, disorder or condition and therefore the disease states, disorders or conditions to which the claim is drawn cannot be determined.

6. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claim is indefinite where a method of treating in a mammal, "age-related cognitive decline" is claimed. It is unclear what diseases, disorders, or conditions is "age-related cognitive decline" includes or excludes. Are Alzheimer disease, Parkinson's disease considered age related or not. No definition of the term is found in the specification. The instant claim is indefinite because the scope of the claim cannot be ascertained due to the ambiguous terminology used.

The term "eating disorder" is indefinite because eating disorder encompassed both over eating and anorexia. A compound treats over eating such as obesity would be detrimental to patients of anorexia.

7. Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear as to what does the term "wherein one or more atoms thereof have an atomic mass or mass number different from the atomic mass or mass number usually found in nature" mean. Please note that an atom has different distribution of isotop naturally. For example the atomic weight of carbon being 12.001 in the periodic table is the average of  $C^{12}$ ,  $C^{13}$ ,  $C^{14}$  in its nature distribution. It is not understood which atom in claim 1 is in its nature atomic mass and which is not. If the claim is intended for radio labeling of an element in claim 1 therefore, the element contain an enhance quantity of certain atomic mass beyond its natural distribution, then, such enhancement of which atom at what location must be described and enabled since to maintain such an enhanced product, the element must be at a position wherein nature exchange does not happed. Therefore, claim 28 is also rejected under 35 U.S.C. 112, first paragraph, as

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failing to comply with the written description requirement as well as failing to comply with the enablement requirement for the above reason.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Please note that modulating an opioid receptor or receptors encompassed both inhibition and enhancement of receptor activity. A single compound cannot both simultaneously inhibit and enhance receptor activity. While the specification provided a Markush group of compounds and a method for testing the compounds' activity with regard to opioid receptors, (see Specification, pages 14-15) no data was provided as to which Markush combination would render inhibitory activity and which Markush combination would render enhancement activity. Absent of each description, which is essential for support of the claims to encompass the diversified disorders as listed on pages 7-8, the specification lacks sufficient description for the instant claim.

9. Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01(a) "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

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The factors to be considered herein are those set forth as the *In re Wands*, 8 USPQ 2<sup>nd</sup> 1400 (1988) decision.

Nature of Invention

The instant claim is drawn to a method of treating in a mammal, in need thereof, a disease state, disorder or condition mediated by an opioid receptor or receptors which method comprises administering to said mammal an amount of a compound according to claim 1 effective in modulating an opioid receptor or receptors.

The State of the art and Predictability

It is well known in the art that the opioid receptor is not a single receptor, but rather a family of receptors (see CA 130:346635). The function of opioid receptors is extremely complex and varies throughout different physiological states (see CA 127:341842). Furthermore, other central and peripheral processes may mediate opioid receptor action (see CA 126:54900). It is evidenced throughout the art that the method of manipulating receptor binding, thus subsequently affecting receptor function, is a very complex process with no predictability or generalization.

The amount of guidance and working examples

The specification provided no description of what constitutes mediation and modulation and by what mediation or modulation of which specific receptor will a disease or pathological condition be *inexorably* linked to such mediation or modulation. The specification provided a limited list of various assay procedures for determining opioid receptor activity including a binding assay, GTP gamma S binding assay and tail-flick assay without any data (see Specification, pages 14-15). In absence of any specific substantial support for a specific opioid receptor subtype with a specific testing procedure which is inexorably linked to a specific pathology or disorder, the mere disclosure of multiple assay procedures for diversified receptor function including all antagonistic, agonistic and binding affinity, does not offer one having ordinary skill in the art, how to operate the method without undue experimentation. The disclosure lacks description or enablement as to correlate any property of receptor function with any particular compound. In view of the diversity of multiple utilities as illustrated on pages 7-8, and the high degree of complexity and unpredictability for the opioid receptor family known in

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the art, the specification offer one of ordinary skill in the art no description or guidance on how to use the compounds in the instant claimed method.

10. Claims 22-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01(a) "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." The factors to be considered herein are those set forth as the *In re Wands*, 8 USPQ 2<sup>nd</sup> 1400 (1988) decision.

#### Nature of Invention

Claims 22-24 are drawn to a method for treating such a diversity and conflicting of disorders for example eating disorder (both obesity and norexia), depression, schizophrenia, irritable bowel syndrome, Parkinson's disease, Alzheimer's disease, drug addition, etc. in a mammal in need thereof comprising administering to said mammal, an amount of a compound according to claim 1 effective in treating said disease state, disorder or condition. No nexus exists among the diversity of such disorders which have multiple and unrelated etiology.

#### The State of the art and Predictability

Treating eating disorder both obesity and anorexia can not be accomplished because compounds active in one would be detrimental to another.

Furthermore, the state of the art in treating eating disorders is extremely complex and treatment methods are highly specific to the patient being treated. "The eating disorders remain perplexing treatment challenges" (see Wiseman et al., "Eating Disorders", Med. Clin. North Am., 1998, 82/1, abstract). "Treatment, accordingly, should be comprehensive, individualized, and multifaceted" (see Wells, et al., Curr. Opin. Pediatr., 2001, 13/6, abstract). Finally, the affect of medication on eating disorders is yet to be determined. "In the treatment of anorexia nervosa, there is little evidence that psychotropic medications, including antipsychotic agents,



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antidepressants, and cyproheptadine, are of significant benefit to most patients who are in the acute phase of treatment and are receiving behavioral treatment to promote weight gain...The role of medication in the treatment of binge eating among the obese remains to be determined” (see Walsh et al., Child Adolesc. Psychiatr. Clin. North Am., 1995, 4/2, abstract).

Treating a neurological disorder such as neurodegenerative disease, including those such as Alzheimer’s disease, Parkinson’s disease, etc. has been well recognized in the art to be literally untreatable (see CA 126:324757). In addition, in so far as neuropathies are concerned, it is well recognized that many neuropathies have different etiology and treatment of such conditions is highly specific. In absence of specific description of enablement, one skilled in the art is unable to operate such process (see CA 127:174580).

Also, for the CNS related neurological disorders, it is a well-known fact that any compound having CNS efficacy must cross the blood brain barrier. No description for the instant claimed compounds having the ability to cross the blood-brain barrier has been provided.

The amount of guidance and working examples

No data or examples were provided for any compound as claimed in claim 1 illustrating which compound was effective with respect to specific disorders in order to guide one having ordinary skill in the art to pick and choose for the individual method of treatment.

In view of the absolute requirement for a compound to cross the blood-brain barrier in order for it to have efficacy in the CNS, no description or enablement can be found that the claimed compound would have any practical CNS method of use.

There isn’t any one etiological mechanism that can treat such a diversity of diseases as those of the instant claims 22-24. Also, there is no description of which compounds according to claim 1 inhibit particular opioid receptors and which compounds enhance particular opioid receptors nor is there written description illustrating a nexus between the stated disease states, disorders or conditions and inhibition or enhancement of specific opioid receptors. No support was found that any of the compounds are able treat any pathology or symptom, nor was any pathology or symptom inexorably linked to inhibition or enhancement of opioid receptors.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 9 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by CA 2,309,434.

See examples 2-14, 16, 18-19 anticipated the instant claims wherein R1 and R2 are hydrogen or alkyl or (CH<sub>2</sub>)<sub>k</sub>-aryl, R6 and R7 are methyl, X is H, R3 or R5 are H or alkyl compounds.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7, 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over CA 2,309,434.

Anticipatory compound against claims 1-6, 9 have been clearly pointed out. The difference between the compounds wherein R4 is hydroxyl substituted alkyl is prima facie obvious because the exemplified compounds (2-14, 16, 18-19) have the R3 of the CA 2,309,434 being alkyl. Generically, CA 2,309,434 taught that alkyl or hydroxyl substituted alkyl are optional choice for such compounds (see p. 4, lines 10-13). In absence of unexpected results, there is nothing unobvious in choosing some among many. In re Lemin 141 USPQ 814.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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Claims 1-6, 20-24, 28 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2004/0186135 (see page 27, compound 27 and page 43, compound 33, page 46 compound 41 and 43, page 47, compound 45). The reference anticipated the instant claimed compound wherein R3 and R5 are both hydrogen, X is hydrogen, R6 and R7 are both methyl, n=0, R4 is hydrogen and one of R<sup>1</sup> or R<sup>2</sup> is (CH<sub>2</sub>)<sub>k</sub>aryl-substituted by R<sup>12</sup> wherein R<sup>12</sup> is aryl, halogen or OR<sup>13</sup> wherein R<sup>13</sup> is (CH<sub>2</sub>)<sub>v</sub>NR<sup>16</sup>R<sup>17</sup>, or one of R<sup>1</sup> or R<sup>2</sup> is alkyl(including cyclic, p.10, lines 25-26)-substituted with CO-OR<sup>13</sup>, R<sup>13</sup> is alkyl.

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6, 20-24, 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2004/0186135.

Anticipatory compounds against compounds of the claims wherein one of R<sup>1</sup> or R<sup>2</sup> is (CH<sub>2</sub>)<sub>k</sub>aryl-substituted have been clearly identified supra. The broader scope of the claims wherein one of R<sup>1</sup> or R<sup>2</sup> is (CH<sub>2</sub>)<sub>k</sub>heteroaryl or cycloalkyl have been generically described (see pages 2-3, formula I) and the optional alternative variation have been guided by the examples see examples 47-49.

15. Claims 1-7, 10, 20-24 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2005/0222204 (see claims 1-9, 11-12). The reference anticipated the instant claimed compound wherein R3=R5=X=R4=hydrogen, R6 and R7 are both methyl, n=0, 1 or 2, one of R1 or R2 is an alkyl group substituted with two R12 groups wherein one R12 is OR13 and R13 is hydrogen and the other R12 group is a C6 cycloalkyl and one of R1 and R2 is hydrogen.

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16. Claims 1-6, 9, 20-24 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2005/0222204 (see page 7, Table I, formula II). The reference anticipated the instant claimed compound wherein  $R_3=R_5=X=R_4$ =hydrogen,  $R_6$  and  $R_7$  are both methyl,  $n=0-5$  one of  $R_1$  or  $R_2$  is an alkyl group and one of  $R_1$  and  $R_2$  is hydrogen.

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7, 9-10, 20-24, 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Armer CA 2,309,434 in view of Zimmerman et al. US 4,891,379.

Determination of the scope and content of the prior art (MPEP § 2141.01)

Armer CA '434 disclosed anticipating compounds against claims 1-6, 9, 20-24, 28 as delineated supra in section 11 which is hereby incorporated by reference.

Ascertainment of the difference between the prior art and the claims (MPEP § 2141.02)

The difference between Armer '434 and the instant claims is that the more limited claimed compounds have the  $R_4$  being hydroxyl for which an example to this attribute was not exemplified (see section 12). Zimmerman et al. '379 is analogous art wherein the analogous compounds for the same utility was disclosed. Zimmerman et al. '379 provided that in analogous compounds, the 1-hexyl moieties of Armer compounds would have similar activity upon substitution with a hydroxyl group (see col. 20 example 30).

Finding of prima facie obviousness-rationale and motivation (MPEP § 2142-2143)

One having ordinary skill in the art in possession of Armer '434 and Zimmerman et al., US 4,891,379 (see columns 1-2, column 23 and column 32, claims 1-5) would be motivated to modify the Armer et al. '434 compounds with a hydroxyl substitution **because** one skilled in the art is deemed to be aware of all the pertinent art in the filed. The Zimmerman et al. '379

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provided guidance on picking the generically disclosed attributes of Armer for such opioid receptor binding compounds.

18. Claims 1-7, 9-10, 20-4, 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitch et al. US 2005/0222204 in view of Dolle et al. US 2004/0186135.

Determination of the scope and content of the prior art (MPEP § 2141.01)

Mitch et al. disclosed an anticipatory compound against the claims, 1-7, 10, 20-24, 28, as delineated, see 2005/0222204, page 7, Table I, formula I and II.

Ascertainment of the difference between the prior art and the claims (MPEP § 2141.02)

The difference between the instant claim 9 and the reference compound is that instead of  $n=1$ , the reference disclosed  $n=2$  compounds (see claims 1-9, 11-12).

Finding of prima facie obviousness-rationale and motivation (MPEP § 2142-2143)

One having ordinary skill in the art in possession of the Mitch '204 would be motivated to modify the linking chain with  $n=2$  to  $n=1$  because in analogous art by Dolle '135 it was generically disclosed that the R4 moiety can be optionally a cycloalkyl or  $C_{1-10}$ alkylsubstituted cycloalkyl (see page 53, right column R4 definitions) with particular guidance that variation of chain linker would not have affected the biological activity (see example p.42 compound 30 or p.50 compound 54 vs page 48 compound 49).

19. None of the claims are allowed.


20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Sarah E. Perlinger, whose telephone number is (571) 272-5574. The examiner can normally be reached on Monday through Friday, 8:30 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Thomas McKenzie, can be reached at (571) 272-0670. The fax number for the organization where this application or proceeding is assigned is (571)-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*OACS/Chang*  
*Mar. 12, 2007*

  
*Celia Chang*  
*Primary Examiner*  
*Art unit 1625*